REMARKS

Status Summary

Claims 11-13 and 16-42 are pending in the application. Claims 11-13, 16-23, 25-30, and 35-40 are withdrawn from consideration as directed to non-elected inventions, and claims 1-10 and 14-15 were canceled previously. Claims 24, 31-34, and 41-42 were examined with respect to the elected species of a method of using the antibody to deplete B cells. Based upon the supplemental election response dated June 6, 2003, the examiner has decided to examine both the species of SEQ ID NO:7 (2B8 variable region light chain) and SEQ ID NO:11 (2B8 variable region heavy chain).

Claim 24 is amended. Claims 11-13, 16-23, 25-30, and 35-40 are canceled without prejudice. New claims 43-44 are added. Reconsideration is respectfully requested in view of the amendments and following remarks.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 24, 31-34, and 41-42 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. With respect to claim 24, the examiner contends that the specification lacks support for the phrase "in a patient in need of such depletion." In particular, the examiner states that the specification does not disclose the scope of the claimed invention which encompasses methods for treating conditions other than B cell disorders, such as the use of B cell depletion to prevent a normal immune response against an administered antigen. Official action, page 2, item 5. This rejection is respectfully traversed.

Claim 24 is also rejected under § 112, first paragraph, as allegedly unsupported in use of the language "merely complete B cell depletion with about 24 hours post treatment." Aside from the obvious typos, the examiner notes that although the specification supports *nearly* complete depletion of peripheral B cells *within* about 24 hours, nearly complete depletion of B cells other than peripheral B cells, *e.g.*, B cells in the lymph nodes, is not described. Official action, page 3, cont. item 5. This rejection is also traversed.

In response to the first basis for rejection, claim 24 is amended to specify treatment of a patient having a B cell disorder. Support for the amendment is found in the application as originally filed, including at page 9, lines 10-17, wherein it is described that the disclosed therapeutic methods are designed for the treatment of B cell disorders; and at page 14, lines

10-12, wherein it is described that the present invention is a therapeutic approach to B cell disorders, which involves purging of peripheral B cells using chimeric anti-CD20 antibodies.

In response to the second basis for rejection, claim 24 is further amended to specify depletion of peripheral B cells, more particularly, depletion of at least 90% of peripheral B cells. Support for the amendment can be found in the application as originally filed, including, for example, in Figure 9A, wherein the level of B cells decreases by about 90% at day 0 post infusion; at page 15, lines 25-26, wherein it is described that the depletion of B cell is nearly complete within about 24 hours post infusion; at page 49, lines 12-16, wherein it is described that there was a dramatic decrease (>95%) in peripheral B cells following administration of chimeric anti-CD20 antibody (*see also* Figure 9); and at page 51, wherein Table I shows that >90% of peripheral B cells were depleted in each of subjects C and D following a single dose administration of chimeric anti-CD20 antibody.

As explained above, claim 24 is believed to fully describe the invention as required under 35 U.S.C. § 112, first paragraph. Claims 31-34 and 41-42 ultimately depend from claim 24 and thus also include the above-noted elements of amended claim 24. Based on the foregoing, withdrawal of the rejection of claims 24, 31-34, and 41-42 is respectfully requested.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph – NewMatter

Claims 31-32 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter. Specifically, the examiner states that the specification does not disclose the use of chimeric antibodies that contain the heavy chain of claim 31 in combination with any light chain, nor the heavy chain of claim 32 in combination with any light chain. Rather, in the view of the examiner, the specification discloses only the use of the C2B8 antibody, which contains both the heavy and light chains of claims 31 and 32, respectively. Official action, page 3, item 6. This rejection is respectfully traversed.

Claim 31 is directed to use of any antibody of the genus of antibodies having a variable region heavy chain of SEQ ID NO:11, such as the C2B8 antibody, and which is capable of depleting greater than 90% of peripheral B cells following a single administration at the specified dose. Similarly, claim 32 is directed to use of any antibody of the genus of antibodies having a variable region light chain of SEQ ID NO:7, including the C2B8 antibody, which has the specified B cell depleting activity. The originally filed application describes the genus of antibodies of each of claims 31-32, for example at page 14, lines 10-12, wherein the use of chimeric anti-CD20 antibodies is generically described; at page 12, line 23, through

page 13, line 11, wherein the antigen-binding properties of chimeric anti-CD20 antibodies is described; and at page 19, line 22, through page 20, line 5, wherein it is described that the variable region light and heavy chains can be separately expressed for subsequent antibody assembly. As stated in the cited paragraphs, and *exemplified* by preparation of the C2B8 antibody, anti-CD20 antibodies are readily prepared using recombinant DNA cloning techniques.

Based on the foregoing, claims 31-32 are believed to be fully supported by the originally filed specification. Thus, claims 31-32 do not constitute new matter and withdrawal of the rejection of claims on this basis is respectfully requested.

To more particularly claim use of the C2B8 antibody, new claim 43 is directed to use of a chimeric anti-CD20 antibody containing the variable region heavy chain of SEQ ID NO:11 and the variable region light chain of SEQ ID NO:7, or CD20 binding fragment thereof. Similarly, new claim 44 is directed to use of a chimeric anti-CD20 antibody containing the complementarity regions of SEQ ID NOs: 7 and 11, as depicted in Figures 4 and 5. As stated above, a skilled artisan could readily prepare such an antibody based on the instant disclosure and standard molecular cloning techniques.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 24, 31-34, and 41-42 are further rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to enable practice of a method for nearly complete depletion of B cells other than peripheral B cells. In support of this rejection, the examiner points to results presented in Table II of the specification (page 53) as showing only marginal B cell depletion from lymph nodes 7 days after treatment. Official action, pages 3-4, item 7. This rejection is respectfully traversed.

As noted above in response to the rejection of claims as allegedly lacking sufficient written description, claim 24 is amended to specify depletion of peripheral B cells. Based thereon, claim 24 and dependent claims 31-34 and 41-42 are believed to fully comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, and therefore withdrawal of this rejection is respectfully requested.

Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Claims 24, 31-34, and 41-42 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite in use of the same language, *i.e.*, "[nearly] complete B cell depletion."

The examiner contends that this description is unclear in lacking a quantitative measure. Official action, page 4, item 8.

Also noted above in response to the rejection of claims under 35 U.S.C. § 112, first paragraph, claim 24 is amended to specify depletion of greater than 90% of peripheral B cells. This quantitative measure of B cell depletion is believed to more particularly point out the claimed invention in compliance with 35 U.S.C. § 112, second paragraph, and thus withdrawal of this rejection is respectfully requested.

Conclusion

All objections and rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If any points remain in issue, which the examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

PILLSBURY WINTHROP LLP

Thomas A. Cawley, Jr., Ph.D.
Registration No. 40,944

P.O. Box 10500
McLean, VA 22102
(703) 905-2144 Direct Dial
(703) 905-2500 Facsimile

December 3, 2003

TAC/JBM